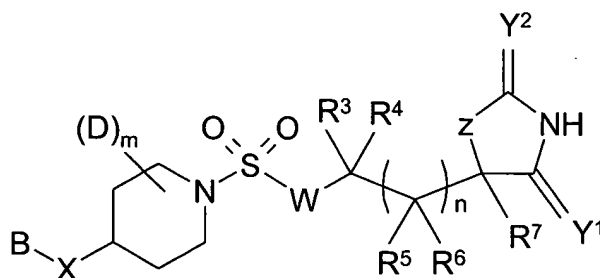


Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (Currently amended) A compound of formula (1) or a pharmaceutically acceptable salt thereof:



formula (1)

wherein:

Y¹ and **Y²** are independently O or S;

z is NR⁸, O or S;

n is 0 or 1;

W is NR¹, CR¹R² or a bond;

m is 0 or 1;

D is hydrogen, C₁₋₄alkyl, C₃₋₆cycloalkyl or fluoro;

X is -(CR¹²R¹³)_t-Q-(CR¹⁴R¹⁵)_u- where t and u are independently 0 or 1 and Q is O, S, SO or SO₂;

B is a group selected from aryl, heteroaryl and heterocyclyl, where each group is optionally substituted by one or more groups independently selected from nitro, trifluoromethyl, trifluoromethoxy, halo, cyano, C₁₋₄alkyl (optionally substituted by R⁹ or C₁₋₄alkoxy or one or

more halo}, C₂₋₄alkenyl (optionally substituted by halo or R⁹), C₂₋₄alkynyl (optionally substituted by halo or R⁹), C₃₋₆cycloalkyl (optionally substituted by R⁹ or one or more halo), C₅₋₆cycloalkenyl (optionally substituted by halo or R⁹), aryl (optionally substituted by halo or C₁₋₄alkyl), heteroaryl (optionally substituted by halo or C₁₋₄alkyl), heterocyclyl (optionally substituted by C₁₋₄alkyl), -SR¹¹, -SOR¹¹, -SO₂R¹¹, -SO₂NR⁹R¹⁰, -NR⁹SO₂R¹¹, -NHCONR⁹R¹⁰, -OR⁹, -NR⁹R¹⁰, -CONR⁹R¹⁰ and -NR⁹COR¹⁰; or B is C₂₋₄alkenyl or C₂₋₄alkynyl, each being optionally substituted by a group selected from C₁₋₄alkyl, C₃₋₆cycloalkyl, aryl, heteroaryl and heterocyclyl which group is optionally substituted by one or more halo, nitro, cyano, trifluoromethyl, trifluoromethoxy, -CONHR⁹, -CONR⁹R¹⁰, -SO₂R¹¹, -SO₂NR⁹R¹⁰, -NR⁹SO₂R¹¹, C₁₋₄alkyl or C₁₋₄alkoxy; with the provisos that:

when n is 1 and W is NR¹, CR¹R² or a bond; or when n is 0 and W is CR¹R²; then B is a group selected from aryl, heteroaryl and heterocyclyl, where each group is optionally substituted by one or more groups independently selected from nitro, trifluoromethyl, trifluoromethoxy, halo, cyano, C₁₋₄alkyl (optionally substituted by R⁹ or C₁₋₄alkoxy or one or more halo), C₂₋₄alkenyl (optionally substituted by halo or R⁹), C₂₋₄alkynyl (optionally substituted by halo or R⁹), C₃₋₆cycloalkyl (optionally substituted by R⁹ or one or more halo), C₅₋₆cycloalkenyl (optionally substituted by halo or R⁹), aryl (optionally substituted by halo or C₁₋₄alkyl), heteroaryl (optionally substituted by halo or C₁₋₄alkyl), heterocyclyl (optionally substituted by C₁₋₄alkyl), -SR¹¹, -SOR¹¹, -SO₂R¹¹, -SO₂NR⁹R¹⁰, -NR⁹SO₂R¹¹, -NHCONR⁹R¹⁰, -OR⁹, -NR⁹R¹⁰, -CONR⁹R¹⁰ and -NR⁹COR¹⁰; or B is C₂₋₄alkenyl or C₂₋₄alkynyl, each being optionally substituted by a group selected from C₁₋₄alkyl, C₃₋₆cycloalkyl, aryl, heteroaryl and heterocyclyl which group is optionally substituted by one or more halo, nitro, cyano, trifluoromethyl, trifluoromethoxy, -CONHR⁹, -CONR⁹R¹⁰, -SO₂R¹¹, -SO₂NR⁹R¹⁰, -NR⁹SO₂R¹¹, C₁₋₄alkyl or C₁₋₄alkoxy; and when n is 0 and W is NR¹ or a bond; then B is a group selected from bicyclic aryl, bicyclic heteroaryl and bicyclic heterocyclyl, where each group is optionally substituted by one or more groups independently selected from nitro, trifluoromethyl, trifluoromethoxy, halo, cyano, C₁₋₄alkyl (optionally substituted by R⁹ or C₁₋₄alkoxy or one or more halo), C₂₋₄alkenyl (optionally substituted by halo or R⁹), C₂₋₄alkynyl (optionally substituted by halo or R⁹), C₃₋₆cycloalkyl

(optionally substituted by R^9 or one or more halo), C_{5-6} cycloalkenyl (optionally substituted by halo or R^9), aryl (optionally substituted by halo or C_{1-4} alkyl), heteroaryl (optionally substituted by halo or C_{1-4} alkyl), heterocyclyl (optionally substituted by C_{1-4} alkyl), $-SR^{11}$, $-SOR^{11}$, $-SO_2R^{11}$, $-SO_2NR^9R^{10}$, $-NR^9SO_2R^{11}$, $-NHCONR^9R^{10}$, $-OR^9$, $-NR^9R^{10}$, $-CONR^9R^{10}$ and $-NR^9COR^{10}$; or B is C_{2-4} alkenyl or C_{2-4} alkynyl, each being optionally substituted by a group selected from C_{1-4} alkyl, C_{3-6} cycloalkyl, aryl, heteroaryl and heterocyclyl which group is optionally substituted by one or more halo, nitro, cyano, trifluoromethyl, trifluoromethoxy, $-CONHR^9$, $-CONR^9R^{10}$, $-SO_2R^{11}$, $-SO_2NR^9R^{10}$, $-NR^9SO_2R^{11}$, C_{1-4} alkyl or C_{1-4} alkoxy;

R^1 and R^2 are independently hydrogen or a group selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} cycloalkyl and C_{5-6} cycloalkenyl which group may be optionally substituted by halo, cyano, hydroxy or C_{1-4} alkoxy;

R^3 , R^4 , R^5 and R^6 are independently hydrogen or a group selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-6} cycloalkyl, C_{5-6} cycloalkenyl, aryl, heteroaryl and heterocyclyl which group is optionally substituted by one or more substituents independently selected from halo, nitro, cyano, trifluoromethyl, trifluoromethoxy, C_{1-4} alkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{3-6} cycloalkyl (optionally substituted by one or more R^{17}), aryl (optionally substituted by one or more R^{17}), heteroaryl (optionally substituted by one or more R^{17}), heterocyclyl, $-OR^{18}$, $-SR^{19}$, $-SOR^{19}$, $-SO_2R^{19}$, $-COR^{19}$, $-CO_2R^{18}$, $-CONR^{18}R^{20}$, $-NR^{16}COR^{18}$, $-SO_2NR^{18}R^{20}$ and $-NR^{16}SO_2R^{19}$; or R^1 and R^3 together with the nitrogen or carbon atoms and carbon atom to which they are respectively attached form a saturated 3- to 7-membered ring optionally containing 1 or 2 heteroatom groups selected from NH, O, S, SO and SO_2 where the ring is optionally substituted on carbon by C_{1-4} alkyl, fluoro or C_{1-4} alkoxy and/or on nitrogen by $-COC_{1-3}$ alkyl, $-SO_2C_{1-3}$ alkyl or C_{1-4} alkyl;

or R^3 and R^4 together form a saturated 3- to 7-membered ring optionally containing 1 or 2 heteroatom groups selected from NH, O, S, SO and SO_2 where the ring is optionally substituted on carbon by C_{1-4} alkyl, fluoro or C_{1-4} alkoxy and/or on nitrogen by $-COC_{1-3}$ alkyl, $-SO_2C_{1-3}$ alkyl or C_{1-4} alkyl;

or R^5 and R^6 together form a saturated 3- to 7-membered ring optionally containing 1 or 2 heteroatom groups selected from NH, O, S, SO and SO₂ where the ring is optionally substituted on carbon by C₁₋₄alkyl, fluoro or C₁₋₄alkoxy and/or on nitrogen by -COC₁₋₃alkyl, -SO₂C₁₋₃alkyl or C₁₋₄alkyl;

R^7 is hydrogen or a group selected from C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, heteroalkyl, C₃₋₇cycloalkyl, aryl, heteroaryl or heterocyclyl where the group is optionally substituted by halo, C₁₋₄alkyl, C₁₋₄alkoxy, C₃₋₇cycloalkyl, heterocyclyl, aryl, heteroaryl or heteroalkyl; and wherein the group from which R^7 may be selected is optionally substituted on the group and/or on its optional substituent by one or more substituents independently selected from halo, cyano, C₁₋₄alkyl, nitro, haloC₁₋₄alkyl, heteroalkyl, aryl, heteroaryl, hydroxyC₁₋₄alkyl, C₃₋₇cycloalkyl, heterocyclyl, C₁₋₄alkoxyC₁₋₄alkyl, haloC₁₋₄alkoxyC₁₋₄alkyl, -COC₁₋₄alkyl, -OR²¹, -CO₂R²¹, -SR²⁵, -SOR²⁵, -SO₂R²⁵, -NR²¹COR²², -CONR²¹R²² and -NHCONR²¹R²²;

or R^3 and R^7 together with the carbon atoms to which they are each attached and (CR⁵R⁶)_n form a saturated 5- to 7-membered ring optionally containing a heteroatom group selected from NH, O, S, SO and SO₂ where the ring is optionally substituted on carbon by C₁₋₄alkyl, fluoro or C₁₋₄alkoxy and/or on nitrogen by -COC₁₋₃alkyl, -SO₂C₁₋₃alkyl or C₁₋₄alkyl;

R^8 is selected from hydrogen, C₁₋₆alkyl and haloC₁₋₆alkyl;

R^9 and R^{10} are independently hydrogen, C₁₋₆alkyl or C₃₋₆cycloalkyl;

or R^9 and R^{10} together with the nitrogen to which they are attached form a heterocyclic 4 to 7-membered ring.

R^{11} is C₁₋₆alkyl or C₃₋₆cycloalkyl;

R^{12} , R^{13} , R^{14} and R^{15} are independently selected from hydrogen, C₁₋₆alkyl and C₃₋₆cycloalkyl;

R^{16} is hydrogen or C₁₋₆alkyl;

R^{17} is selected from halo, C₁₋₆alkyl, C₃₋₆cycloalkyl and C₁₋₆alkoxy;

R^{18} is hydrogen or a group selected from C₁₋₆alkyl, C₃₋₆cycloalkyl, C₅₋₇cycloalkenyl, saturated heterocyclyl, aryl, heteroaryl, arylC₁₋₄alkyl and heteroarylC₁₋₄alkyl which group is optionally substituted by one or more halo;

R^{19} and R^{25} are independently a group selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{5-7} cycloalkenyl, saturated heterocyclyl, aryl, heteroaryl, aryl C_{1-4} alkyl and heteroaryl C_{1-4} alkyl which group is optionally substituted by one or more halo;

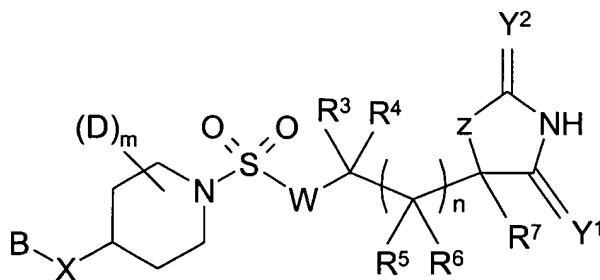
R^{20} is hydrogen, C_{1-6} alkyl or C_{3-6} cycloalkyl;

or R^{18} and R^{20} together with the nitrogen to which they are attached form a heterocyclic 4- to 7-membered ring;

R^{21} and R^{22} are independently hydrogen, C_{1-4} alkyl, halo C_{1-4} alkyl, aryl and aryl C_{1-4} alkyl;

or R^{21} and R^{22} together with the nitrogen to which they are attached form a heterocyclic 5- to 6-membered ring.

2. (Currently amended) A compound of formula (1) or a pharmaceutically acceptable salt thereof:



wherein:

Y^1 and Y^2 are independently O or S;

z is NR^8 , O or S;

n is 0;

W is NR^1 ;

m is 0 or 1;

D is hydrogen, C_{1-4} alkyl, C_{3-6} cycloalkyl or fluoro;

X is $-(CR^{12}R^{13})_t-Q-(CR^{14}R^{15})_u-$ where t and u are independently 0 or 1 and Q is O, S, SO or SO₂;

B is a group selected from aryl, heteroaryl and heterocyclyl, where each group is optionally substituted by one or more groups independently selected from nitro, trifluoromethyl,

trifluoromethoxy, halo, cyano, C₁₋₄alkyl (optionally substituted by R⁹ or C₁₋₄alkoxy or one or more halo), C₂₋₄alkenyl (optionally substituted by halo or R⁹), C₂₋₄alkynyl (optionally substituted by halo or R⁹), C₃₋₆cycloalkyl (optionally substituted by R⁹ or one or more halo), C₅₋₆cycloalkenyl (optionally substituted by halo or R⁹), aryl (optionally substituted by halo or C₁₋₄alkyl), heteroaryl (optionally substituted by halo or C₁₋₄alkyl), heterocyclyl (optionally substituted by C₁₋₄alkyl), -SR¹¹, -SOR¹¹, -SO₂R¹¹, -SO₂NR⁹R¹⁰, -NR⁹SO₂R¹¹, -NHCONR⁹R¹⁰, -OR⁹, -CONR⁹R¹⁰ and -NR⁹COR¹⁰;

R¹ is hydrogen or a group selected from C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₃₋₆cycloalkyl and C₅₋₆cycloalkenyl which group may be optionally substituted by halo, cyano, hydroxy or C₁₋₄alkoxy;

R³ and R⁴ are independently hydrogen or a group selected from C₁₋₄alkyl, C₂₋₄alkenyl, C₂₋₄alkynyl, C₃₋₅cycloalkyl, pentenyl, aryl, heteroaryl and heterocyclyl which group is optionally substituted by one or more substituents independently selected from halo, nitro, cyano, trifluoromethyl, trifluoromethoxy, C₁₋₄alkyl, C₂₋₄alkenyl, C₂₋₄alkynyl, C₃₋₆cycloalkyl (optionally substituted by one or more R¹⁷), aryl (optionally substituted by one or more R¹⁷), heteroaryl (optionally substituted by one or more R¹⁷), heterocyclyl, -OR¹⁸, -SR¹⁹, -SOR¹⁹, -SO₂R¹⁹, -CONR¹⁸R²⁰ and -NR¹⁶COR¹⁸;

or R¹ and R³ together with the nitrogen and carbon atoms to which they are respectively attached form a saturated 3- to 7-membered ring optionally containing 1 or 2 heteroatom groups selected from NH, O, S, SO and SO₂ where the ring is optionally substituted on carbon by C₁₋₄alkyl, fluoro or C₁₋₄alkoxy and/or on nitrogen by -COC₁₋₃alkyl, -SO₂C₁₋₃alkyl or C₁₋₄alkyl;

or R³ and R⁴ together form a carbocyclic or saturated heterocyclic 3- to 7-membered ring optionally containing 1 or 2 heteroatom groups selected from NH, O, S, SO and SO₂ where the ring is optionally substituted on carbon by C₁₋₄alkyl, fluoro or C₁₋₄alkoxy and/or on nitrogen by -COC₁₋₃alkyl, -SO₂C₁₋₃alkyl or C₁₋₄alkyl;

R⁷ is hydrogen or a group selected from C₁₋₄alkyl, heteroalkyl, C₃₋₅cycloalkyl, aryl, heteroaryl or heterocyclyl which group is optionally substituted by halo, C₁₋₄alkyl, C₁₋₄alkoxy, C₃₋₅cycloalkyl, heterocyclyl, aryl, heteroaryl or heteroalkyl; and wherein the group from which R⁷ may be

selected is optionally substituted on the group and/or on its optional substituent by one or more substituents independently selected from halo, cyano, C₁₋₄alkyl, nitro, haloC₁₋₄alkyl, heteroalkyl, aryl, heteroaryl, hydroxyC₁₋₄alkyl, C₃₋₅cycloalkyl, heterocyclyl, C₁₋₄alkoxyC₁₋₄alkyl, haloC₁₋₄alkoxyC₁₋₄alkyl, -COC₁₋₄alkyl, -OR²¹, -CO₂R²¹, -SR²⁵, -SOR²⁵, -SO₂R²⁵, -CONR²¹R²² and -NHCONR²¹R²²;

or R³ and R⁷ together with the carbon atoms to which they are each attached and (CR⁵R⁶)_n form a saturated carbocyclic or heterocyclic 5- or 6-membered ring;

R⁸ is selected from hydrogen, C₁₋₄alkyl and haloC₁₋₄alkyl;

R⁹ and R¹⁰ are independently hydrogen, C₁₋₆alkyl or C₃₋₆cycloalkyl;

or R⁹ and R¹⁰ together with the nitrogen to which they are attached form a heterocyclic 4 to 6-membered ring.

R¹¹ is C₁₋₄alkyl or C₃₋₅cycloalkyl;

R¹², R¹³, R¹⁴ and R¹⁵ are independently selected from hydrogen, C₁₋₄alkyl and C₃₋₄cycloalkyl;

R¹⁶ is hydrogen or C₁₋₄alkyl;

R¹⁷ is selected from halo, C₁₋₄alkyl, C₃₋₅cycloalkyl and C₁₋₄alkoxy;

R¹⁸ is hydrogen or a group selected from C₁₋₄alkyl, C₃₋₅cycloalkyl, C₅₋₆cycloalkenyl, saturated heterocyclyl, aryl, heteroaryl, arylC₁₋₄alkyl and heteroarylC₁₋₄alkyl which group is optionally substituted by one or more halo;

R¹⁹ and R²⁵ are independently a group selected from C₁₋₄alkyl, C₃₋₅cycloalkyl, C₅₋₆cycloalkenyl, saturated heterocyclyl, aryl, heteroaryl, arylC₁₋₄alkyl and heteroarylC₁₋₄alkyl which group is optionally substituted by one or more halo;

R²⁰ is hydrogen, C₁₋₄alkyl or C₃₋₅cycloalkyl;

or R¹⁸ and R²⁰ together with the nitrogen to which they are attached form a heterocyclic 4- to 6-membered ring;

R²¹ and R²² are independently hydrogen, C₁₋₄alkyl, haloC₁₋₄alkyl, aryl and arylC₁₋₄alkyl;

or R²¹ and R²² together with the nitrogen to which they are attached form a heterocyclic 5- to 6-membered ring.

3. (Currently amended) A compound according to claim 1 wherein B is phenyl, naphthyl, pyridyl, quinolinyl, isoquinolinyl, thienopyridyl, naphthyridinyl, 2,3-methylenedioxyphenyl, 3,4-methylenedioxyphenyl, thienopyrimidinyl, pyridoimidazolyl, benzimidazolyl, benzofuranyl, benzothienyl, indolyl, benzothiazolyl, benzotriazolyl, benzisoxazolyl, benzisothiazolyl, indazolyl, indoliziny, isobenzofuranyl, quinazolinyl, imidazopyridinyl, pyrazolopyridinyl, indolinyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl or isoindolinyl, where each is optionally substituted by one or more groups independently selected from nitro, trifluoromethyl, trifluoromethoxy, halo, C₁₋₄alkyl (optionally substituted by one or more halo), C₂₋₄alkynyl, heteroaryl, -OR⁹, cyano, -NR⁹R¹⁰, -CONR⁹R¹⁰ and -NR⁹COR¹⁰; or B is vinyl or ethynyl optionally substituted by C₁₋₄alkyl.

4. (Currently amended) A compound according to claim 1 ~~or 2~~ wherein B is a group selected from bicyclic aryl, bicyclic heteroaryl and bicyclic heterocyclyl, where each group is optionally substituted by one or more groups independently selected from nitro, trifluoromethyl, trifluoromethoxy, halo, C₁₋₄alkyl (optionally substituted by one or more halo), C₂₋₄alkynyl, heteroaryl, -OR⁹, cyano, -NR⁹R¹⁰, -CONR⁹R¹⁰ and -NR⁹COR¹⁰; or B is C₂₋₄alkenyl or C₂₋₄alkynyl optionally substituted by C₁₋₄alkyl, C₃₋₆cycloalkyl or heterocyclyl.

5. (Currently amended) A compound according to claim 1 ~~or 2~~ wherein B is 2-methylquinolin-4-yl.

6. (Currently amended) A compound according to ~~any one of the preceding claims~~ claim 1 wherein R⁷ is hydrogen or a group selected from C₁₋₄alkyl, arylC₁₋₄alkyl, heteroarylC₁₋₄alkyl, heterocyclylC₁₋₄alkyl, aryl, heteroaryl, heterocyclyl and C₃₋₅cycloalkyl which group is optionally substituted by cyano, C₁₋₄alkyl, halo, -OR²¹, -NR²¹R²², -CO₂R²¹ and -NR²¹CO₂R²².

7. (Original) A compound according to claim 6 wherein R⁷ is hydrogen or C₁₋₄alkyl optionally substituted with halo, hydroxy or C₁₋₃alkoxy.

8. (Currently amended) A pharmaceutical composition comprising a compound according to claim 1 ~~or claim 2~~; and a pharmaceutically-acceptable diluent or carrier.

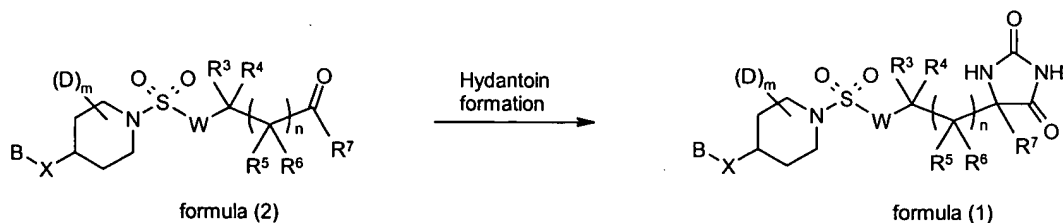
9. (Cancelled)

10. (Currently amended) A method of treating ~~The use of a compound according to claim 1 or 2 in the manufacture of a medicament in the treatment of~~ a disease condition mediated by TNF- α comprising administering to an animal an effective amount of a compound of claim 1.

11. (Cancelled)

12. (Currently amended) A method of treating autoimmune disease, allergic/atopic diseases, transplant rejection, graft versus host disease, cardiovascular disease, reperfusion injury and malignancy ~~in a warm blooded animal, such as man, in need of such treatment~~ which comprises administering ~~to said animal an effective amount of~~ a compound according to claim 1 ~~or 2~~.

13. (Currently amended) A process for preparing a compound according to claim 1 ~~or 2~~, comprising the steps of converting a ketone or aldehyde of formula (2) into a compound of formula (1);



and thereafter if necessary:

- i) converting a compound of formula (1) into another compound of formula (1);
- ii) removing any protecting groups;

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iii) forming a pharmaceutically acceptable salt or *in vivo* hydrolysable ester.